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Monitoring of selected pharmaceuticals over 3 years in a detrital aquifer during artificial groundwater recharge

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Abstract

A screening survey of 81 pharmaceuticals was carried out at a wastewater facility and in a detrital aquifer (Barcelona, Spain), where treated wastewater (TWW) was injected through wells to build up a hydraulic barrier against seawater intrusion. The monitored data correspond to the 2007-2010 period. The TWW was tertiary treated with additional treatment consisting of ultrafiltration, reverse osmosis and UV disinfection. During the monitoring period groundwater monitoring was carried out in wells located within a 1-kilometre radius distance from the injection wells. During monitoring period twenty new pharmaceuticals were detected in the aquifer media and eleven compounds were found with concentration above 0.1 $\mu g l^{-1}$ (selected threshold) in both treated wastewater and wells. After one year of TWW injection change of redox conditions, a decrease of Cl^- concentration and presence of eleven pharmaceuticals (4-AAA, 4-FAA, carbamazepine, ciprofloxacin, diazepam, diclofenac, hydroclorothiazide, mepivacaine, sulfamethoxazole, sulfamethazine and sulfapyridine) was observed in the monitoring wells. After the studied period the sodium-chloride aquifer water type evolved to a bicarbonate-sulphate facies. Decrease of the pharmaceuticals concentration in groundwater appears to be driven by the dilution process and hydraulic characteristics of the aquifer media, being the attenuation or degradation process much less important.

Keywords pharmaceuticals monitoring, groundwater, treated wastewater, hydraulic barrier, detrital aquifer

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Introduction

During the 20th century, a number of chemicals currently used in households, industries, agriculture, or in veterinary and human health were introduced into the environment, many of which are considered persistent. Among them, pharmaceuticals (Phs) are widely used drugs of which more than 4,000 medical compounds are used today (Kümmerer, 2009). The fate and occurrence of these micropollutants in aquatic media is not yet fully understood. They do not need to be persistent to cause negative effects because their transformation or removal is compensated by their continuous introduction into media and by the synergistic effects of complex mixtures being released into the environment (Pomati et al., 2008). For the first time in the European Union, three pharmaceuticals will be included on a "watch list" of emerging pollutants (2011/0429, COD), which could one day be placed on the priority list. The new list acknowledges the risks posed by the three widely used pharmaceuticals: hormonal preparations 17-alphaethinylestradiol and 17-beta-estradiol, and painkiller diclofenac, which is suspected of killing fish.

A vast amount of literature focusing on analytical aspects, removal processes, presence in aquatic media, laboratory experiments, review papers etc., is available (http://www.epa.gov/ppcp/lit.html). Most contributions address wastewater treatment (WWT) to remove these emerging pollutants in effluent water, but also treated wastewater (TWW) reuse is of growing concern. Among the potential uses of reclaimed water, aquifer recharge from treated urban wastewater (flooding, injection) is being increasingly used in areas where water is scarce in order to supplement water resources (Díaz-Cruz and Barceló, 2008) or to form a seawater intrusion barrier (Argo and Cline, 1985). However, although some Phs are partially removed by conventional WWTs, they still may remain in the treated water and in the long term create undesirable effects in aquatic media affecting its final use (Ternes et al., 2002).

The presence of Ph residues in groundwater has been intensively investigated mainly from effluent recharge ponds (Sacher et al., 2001), feedlots (Lindsey et al., 2001; Zhu et al., 2001; Hamscher et al., 2002; Batt et al., 2006), waste control facilities (Andrews et al., 2012; Bartelt_Hunt et al., 2011) and riverbanks (Vogel et al., 2005; Banzhaf et al., 2013). In many cases where geohydrological information is available, antibiotic residues have been detected mainly in shallow phreatic aquifers at depths of 3-6 m below the ground surface (Krapac et al., 2002; Batt et al., 2006).

Much research has focused on the removal of compounds during infiltration through the unsaturated zone (Heberer et al., 2004; Massmann et al., 2006). However, few studies have traced results for recharged TWW directly incorporated into saturated media (groundwater), where attenuation processes

occurring in the unsaturated zone do not occur. The fate of organic contaminants depends on geochemical and nutrient conditions (Lapworth et al., 2012), and low dissolved oxygen/low nutrient conditions favour long-term persistence. A reducing environment has been seen as being important to control the fate and transport of some organic compounds with an otherwise high attenuation potential. While TWW is low in DOM (dissolved organic matter) and is fully oxygenated, DOC (dissolved organic carbon) in wells is low because deep groundwater tends to contain relatively low DOM concentrations (Kaplan and Newbold, 1993). In addition, factors such as porosity, permeability and groundwater velocity control the fate of contaminants.

In previous research from Cabeza et al. (2012) the following pharmaceuticals were detected in the lower Llobregat delta aquifer (Barcelona, Spain) prior to the injection processes (baseline): 4-AA, 4-MAA, codeine, ibuprofen, iopamidol, iopromide, ketorolac, loratadine, paraxanthine and pravastatin. This study attempts to evaluate whether, and to what extent, aquifer quality is affected by the presence of new pharmaceuticals due to artificial recharge from TWW during 2007-2010. Specifically, a screening survey for 81 pharmaceuticals (antibiotics, lipid-regulating agents, analgesic/anti-inflammatory drugs) was conducted in the Llobregat area at different sampling sites. In this area, TWW was injected into aquifer media for seawater intrusion control purposes. The primary objectives of this study were to: (1) determine the distribution of a wide range of pharmaceuticals in the TWW and groundwater receiving these discharges; (2) assess the likelihood of migration through a sand-gravel aquifer using a combination of field observations and literature data; and (3) to investigate hydrochemical changes in aquifer media and pharmaceuticals presence. The secondary objective was to compare the distribution and likely behaviour of compounds in the subsurface environment with those observed in injected waters.

Study area

The study site, the Depurbaix wastewater facility, is located in the Llobregat river delta south-west of the city of Barcelona, NE Spain (see Figure 1). The Depurbaix Wastewater Treatment Plant treats urban wastewater from the southern part of Barcelona and its surroundings, where the population is one million. Before the tertiary treatment a pre-treatment for the elimination of settleable solids and grease, as well as nutrient removal by activated biological sludge was applied. Tertiary treatment consisted of flocculation-coagulation, lamellar clarification followed by filtration and UV disinfection. Before injection into the aquifer, the water received additional treatment: perchloration, ultrafiltration, reverse

osmosis and UV disinfection. A detailed description of the treatment plant facility is presented in Cazurra (2006). The volume of water to be reused at the Depurbaix facility is destined to meet various demands, and one of the objectives is the construction of a hydraulic barrier against sea water intrusion in the Llobregat delta deep aquifer.

From the geological point of view, the Llobregat delta is a Quaternary age formation covering 97 km^2 of unconsolidated sediments of alluvial origin varying from clay to gravel, and it is deposited over blue clay dating back to the Pliocene age, except on the northern boundaries, which overlie older materials. In the delta area, two coastal detrital aquifers (upper and lower) from the quaternary age exist (Fig. 1) but exploitation of the upper aquifer has been abandoned due to the highly polluted water. Research into the lower aquifer has been driven by its value as a strategic water resource for supply, which is the principal objective of all the research conducted (Custodio, 1981). Over the years the intensive exploitation of the deep aquifer has led to the presence of seawater intrusion in different parts, which has recently been made worse by a number of civil work excavations of the impervious layer at the contact between the aquifer and the sea. As a result, groundwater quality has progressively deteriorated, and the possibilities of exploitation have been reduced. Annual surveys have been conducted since the 1960s, when seawater intrusion was first detected.

In 2006, the first hydraulic barrier construction phase was initiated (Ortuño et al., 2008) over an area of above 2.5 km^2 (Fig. 1). The hydraulic barrier scheme consists of injecting TWW, which forms a pressure ridge along the coast to prevent seawater from entering the aquifer. The TWW for the hydraulic barrier consists of the outflow water from the Depurbaix sewage treatment plant, which undergoes the previously described treatment before being stored in a tank for further injection in the lower aquifer through wells.

In the facility, four injection wells (P1 to P4) were constructed prior to the water injection up to a depth of 70 m, and were screened throughout the lower aquifer thickness (59-65 m below the soil surface). The wells are located 1,500 m inland and stand in a line that runs in parallel to the coastline, with a 300-m distance separating each one (Fig. 1). In March 2007, water injection started in P3 and P4, and in P2 in July 2007. Well P4 had to be discarded almost immediately due to technical problems. In July 2008, P1 started functioning. Only wells P1, P2 and P3 were undergoing recharge operations during this first phase. In April 2010, the second barrier phase commenced with 14 injection wells.

During the first phase, the initial injection (620 $m^3 day^{-1}$) consisted of an equal mixture of TWW and tap water from the storage tank. In March 2008, the fraction of tap water was removed and well injection was carried out only with reclaimed water, when the daily volume increased to 2,500 $m^3 day^{-1}$.

Altogether, the system was operating during the monitored period (2007-2010), except for April 26 to July 21 (2008), when the system was out of order due to technical reasons.

The delta aquifers. The lower aquifer

From the hydrogeological point of view, two aquifers are distinguished in the Llobregat delta, the upper unconfined and the deep or lower aquifer, which are separated by a low permeability silt wedge confining the lower, except on the borders of the delta where the silt package pinch out, and the upper and lower aquifers are connected by fine sand layers. Both aquifers are hydraulically connected only on the borders of delta area. In some specific areas however, damaged wells (e.g. corrosion or failure of well casing or screen, improper design or construction) interconnecting the upper and lower aquifers may also exist. The main source of natural recharge comes from the Llobregat river infiltration, mainly in the upper valley, jointly with irrigation water returns to the upper aquifer; discharge is performed through pumping wells and to the sea. The estimated transit time from the river valley recharge to the study area is 10 years (Custodio, 1981).

The aquifer of interest where artificial recharge takes place, the lower one confined by the silt layer, is composed by fine sand and gravel, with an average thickness of 6 m. It almost occupies the entire delta surface, extending under the sea below the silt wedge. The top aquifer depth is generally more than 50 m below the surface soil, and the deepest part of the aquifer's upper limit is 60 m below sea level. The aquifer's hydraulic properties are characterised by significant lateral changes due to the heterogeneity of the lithological facies and the presence of paleochannels; transmissivity values from 100 to 31,000 m^2 day^{-1} have been reported (Iríbar et al., 1997). The transmissivity values from the pumping tests done within the frame of this hydraulic barrier project are 700 and 2,000 m^2day^{-1}, respectively, for the vicinity of wells P1 and P3, whereas for P2 and P4 is 100 and 200 m^2day^{-1}, respectively.

The deep aquifer has been intensively exploited for industrial and water supply, which has led to the lowering piezometric levels. By 1977, the groundwater drawdown reached a maximum of 30 m b.s.l in the centre-right corner of the area; as a result of seawater intrusion maximum chloride concentration in wells was 20,000 mgl^{-1} at the north-eastern part of the aquifer. Before the 1960s the aquifer water type was originally of calcium-bicarbonate composition. At present, the sodium-chloride facies is predominant on approximately two thirds of the aquifer area; piezometric levels in most of the area are below sea level. Since the 1960s, the hydrogeological aspects of the seawater intrusion wedge have

been extensively studied, reflected by a number of reports and publications (Candela et al, 1988; Iríbar et al., 1997, among others).

At the end of the first hydraulic barrier phase (March 2010), the total volume injected into the aquifer accounted for 1.6 Mm^3, leading to quantitative and qualitative changes to groundwater. An average increase in groundwater of 1 m level was observed in the monitored wells (June 2010), being up to 4 m for wells located in the western part of the barrier, favoured by the highest transmissivity of the aquifer. Regarding water quality, the average Cl^- content in sampled wells had been reduced to 350 mgl^{-1}, similar to aquifer values found in not affected areas by seawater intrusion; Electrical Conductivity (EC) and pH was around 1,500 μScm^{-1} and 7.4, respectively. As the aquifer is saturated with the saltwater entering porous media, its cationic composition is expected to be altered by chemical reactions. It is worth to mention that although TWW was oversaturated with calcite, which could implies the possibility of carbonate precipitation in mixing waters, well-clogging problems were not observed.

Materials and methods

Selected pharmaceuticals

The CAS number and use of the 81 selected compounds for monitoring are presented in Table. Basically, their choice was based on the metabolism routes of pharmaceuticals (http://chem.sis.nlm.nih.gov/chemidplus; Lapworth et al., 2012), chemical analysis availability, literature results from previous studies and their ample use. In addition, persistence in aquatic media (i.e., carbamazepine, Gielen, 2007; Banzhaf et al., 2013) and environmental risk were considered (i.e., endocrine disruptors, PAHs; http://ec.europa.eu/research/endocrine/background_disruption_en.html).

Sampling

Sampling the sites for pharmaceuticals consisted of bi-monthly groundwater sample collection from the monitoring network of the Agencia Catalana del Aigua (ACA), and also in injected water into wells P1 to P3. The location of the monitoring and injection wells is shown in Figure 1. The sampling period and groundwater level monitoring covered the March 2007-May 2010 period.

The local groundwater monitoring network for the Llobregat deep aquifer consisted of five wells (RL1 to RL5) and two piezometers (Mp47 and B7-b), located at a distances between 250 m and 800 m to the four injection wells (P1- P4), except Mp47, which was located 4 m from P1. Network monitoring included an initial sampling campaign for the aquifer receiving recharge prior to the TWW injection (March, 2007). All the samples were collected using one litre Teflon-coated amber glass bottles, which were immediately stored in an insulated container chilled with ice packs for shipment to the laboratories. The transit time for sample shipment was less than 24 h.

Monthly water samples were collected in 500 ml glass bottles in order to analyse major ions, physico-chemical parameters (pH, temperature, EC, total dissolved solids (TDS) and total organic carbon content (TOC).

Pharmaceuticals and standard water chemical analyses

The methods used for the pharmaceuticals analyses were based on liquid chromatography-Q-TRAP-Mass Spectrometry. Column: C-18 (3x250 mm, 5µm particle size). Interface polarity: ESI (+) and ESI (-). Mobile phase: ESI (+), water (formic acid 0.1%)/ACN ESI (-), water (0.05% ammonium formate)/CAN and Operation mode: MRM. For detailed information on sample pre-treatment, extraction technique and analytical methods applied, readers are referred to Robles-Molina *et al*. (2014). All the chemical determinations were conducted at the Department of Physical and Analytical Chemistry laboratory, University of Jaen (Spain).

The regulated chemicals, major ion content and physical characteristics of the TWW and groundwater samples were controlled by the ACA, following standard laboratory methods. The *in situ* analysis included pH, EC, redox potential (Eh), dissolved oxygen and temperature. These determinations were made using an in-situ probe Eijelkamp® 18.28.

Aquifer geologic material characterisation

The geologic material from the lower aquifer (at 59-61 and 63-65 m below the soil surface) was collected from three undisturbed soil cores obtained from three wells. Samples were stored in polyethylene bags for transportation and were air-dried prior to any characterisation and testing done in the laboratory. Core samples were thoroughly mixed for the parameters determination.

To characterise porous media, the soil parameters that follow were obtained in the laboratory using

ASTM (1993) standards: bulk density (ρ_d), porosity, grain size distribution, organic matter content, and electric conductivity (μScm^{-1}) at the 1:5 ratio. Soil pH was determined in deionised water at a soil solution ratio of 1:5; for organic matter content, the Walkley and Black method was applied. Cation exchange capacity (CEC; $mmol_c\ kg^{-1}$ of solid) and exchangeable cations were measured using the ammonium/sodium acetate method and the ammonium acetate method, respectively. Mineral content and type of clays were obtained through X-ray diffraction, XRD, from three samples. A Bruker D-5005 X-ray diffractometer was employed with a Cu target tube, and was operated at 40 kV and 30 mA. The EVA software package (Bruker AXS, Germany) and the PDF2 database (ICDD, Denver, USA) were employed for mineral phase identification.

Results and discussion

Aquifer soil-matrix characteristics

Average sediment texture consists of a fairly graded sandy sediment (around 50%) with a strong calcareous composition and a low clay content, with clinochlore and illite being the minerals that dominate the clay fraction; presence of iron or manganese was not detected in the sediment material. Organic carbon was always lower than 0.6 wt%, pH was 8.5 and EC was 272 μScm^{-1} at 25ºC. The CEC value was 22.5 $mmol_c\ kg^{-1}$. Given the aquifer material characteristics, sorption reactions were not expected to be the most important process controlling the fate of the studied compounds (Teijón et al., 2013). Porosity was 0.20 and bulk density was 2.1 g cm^{-3}.

TWW and groundwater major ions characteristics

At the end of the studied period, TWW and groundwater mixture was between 75% and 25% for those wells located in the vicinity of the injection wells characterised by the highest aquifer transmissivity values. The effect of TWW recharge in the aquifer was assessed by monitoring the EC, +Eh and oxidised species changes in wells. Selected parameters are indicators of the groundwater hydrochemical state and they are easily measurable. During the 2007-2010 period, the TWW was characterised by presence of oxidised species, positive Eh values and average EC was 2,000 μScm^{-1}.

In figure 2 concentration of Cl^-, $SO_4^=$ and HCO_3^- in the aquifer media (RL1, RL2 and RL5 wells) with time has been plotted, showing the decrease of measured values in all monitored wells and

monitored period. For well RL5 a marked decrease trend of Cl^- is observed although HCO_3^- concentration remains between 210 and 250 mgl^{-1}. This fact maybe related to aquifer carbonate matrix dissolution, as assessed by the calcite saturation index of groundwater, SI_{cal}. At the initial state of TWW injection groundwater was oversaturated, whereas at the end of the studied period pH increased and water became undersaturated on calcite (SI_{cal} down to -0.2). Nevertheless, HCO_3^- generation by the CH_4 oxidation to CO_2 should not be overestimated. After the studied period the sodium-chloride aquifer water type evolved to a bicarbonate-sulphate facies, as shown by the Stiff diagrams (Fig. 3).

Pharmaceutically active compounds found in TWW and groundwater

The analysis of Phs presence was based on the results obtained from the wells RL1, RL2, RL3 and RL5. Data from piezometer B-7b were considered inaccurate and were consequently eliminated; its spatial location in the aquifer media might explain this fact. The records available for MP47, located 4 m from well P1, extended only to May 2009 (injection started in April 2008) and they were not considered for further analysis considering the short monitored period. However, based on a visual data inspection (not shown here), the effects of injection were immediately reflected in the groundwater composition due to the small distance between the well and the piezometer.

It was considered that the EC decrease in groundwater samples was not only an indicator of the injected water breakthrough in the monitoring wells, but also a good travel time estimation to the wells. Also, presence of the persistent anticonvulsant carbamazepine in the wells was considered an indicator of the injected water front. Carbamazepine undergoes low degradation/biodegradation, and little or no sorption takes place in water sediment systems due to a limited interaction with the negatively charged mineral surfaces in aquifer materials, irrespectively of the redox state (Gielen, 2007, Bertelkamp et al., 2012). The baseline concentration of carbamazepine was found to be below the detection limit (Cabeza et al., 2012). The travel time to the RL1, RL2 and RL5 wells was estimated to be approximately 1 year, while for RL3, located around 200 m south of RL1, injected water was detected around 2 years later of initial injection. The geometry and heterogeneity of the delta aquifer, the paleochannels spatial distribution and the lowest transmissivity on P2 well (100 m^2day^{-1}) may explain the observed differences in travel times.

As presented in Table 1, among the selected pharmaceuticals, 62 active compounds were found at least in one sample water at concentrations ranging between detection and quantification limits (ngl^{-1}). Some pharmaceuticals were not eliminated after the wastewater treatment and were still at detectable

concentration levels. Ten compounds (4-AA, 4-MAA, codeine, ibuprofen, iopamidol, iopromide, ketorolac, loratadine, paraxanthine and pravastatin, Tables 1, 2) were removed after the tertiary and additional treatment of influent water being detected only in groundwater samples.

Four targeted compounds (acetaminophen/paracetamol-analgesic, amitriptyline-antidepressant, azithromycin-antibiotic, ranitidine-histamine H2-receptor drug; see Table 1) were occasionally detected at low concentration values in TWW samples. Seasonality of detected compounds in the TWW was not observed. The increase in compounds concentration at some time periods may be associated with either their greater consumption or the possible failures linked to the treatment plant. Decrease of concentration during treatment was not targeted as we were interested primarily in the subsurface behaviour of compounds due to injection.

Table 2 presents all the pharmaceuticals found at detectable concentration (>0.1μgl^{-1}, threshold concentration selected for analysis of results) in the TWW being injected and groundwater samples during the study period. Minimum, maximum and average concentration is also calculated. Discarding Phs only detected in groundwater: caffeine, ciprofloxacin, diclofenac, erythromycin, gemfibrozil, 4-AAA, naproxen, 4-FAA and ofloxacin present the maximum concentration values, greater than 400 ngl^{-1} in both type of waters.

Although during the study period obtained results show that 20 new Phs were not eliminated during the treatment in the plant, being introduced through the injection wells in aquifer media, only eleven compounds were detected in both the TWW and in monitoring wells. These were: carbamazepine, ciprofloxacin, diazepam, diclofenac, hydroclorothiazide, mepivacaine, 4-AAA, 4-FAA, sulfamethoxazole, sulfamethazine and sulfapyridine. In RL1 well ciprofloxacin instead of sulfamethoxazole was detected. The eleven pharmaceuticals have different functional groups and acid/basic properties, and belong to the antibiotics, nonsteroidal anti-inflammatory drugs-NSAIDs, anxiolytic and diuretics groups of action. Loos et al. (2010) also reported a frequency of detection of 42% and 24% for carbamazepine and sulfamethoxazole, in European groundwater.

Compounds in RL5 and RL2 wells displayed similar breakthrough (with small retardation for RL2) and range of concentration values, being much lower in RL1 (Fig. 4). For RL3, due to longer travel time of injected water, compounds were detected since May 2008 and only 1-year of monitoring period was available. The most persistent pharmaceuticals detected in wells were: 4-AAA, carbamazepine, 4-FAA and hydroclorothiazide. For all of them, concentrations were significantly lower than TWW but greater than 100 ngl^{-1}.

Carbamazepine, a widely used pharmaceutical of the amide group, was detected in all the monitoring wells, with a maximum concentration of 134 ngl^{-1} in RL5 being of 169 ngl^{-1} in injected TWW. It is one of the most frequently detected compounds in groundwater and is highly persistent given the nature of the molecule (neutral and resistance to hydrolysis), as laboratory and field experiments have stated (Drewes et al., 2003; Chefetz et al., 2008); its presence in groundwater has reported by a number of researchers (Sacher et al., 2001; Rabiet et al., 2006; Loos et al., 2010; Fram and Belitz, 2011, among others). High concentrations of 4-AAA and 4-FAA (metabolites of metamizol, a phenazone-type compound) have been also found by Massmann et al. (2006) in mixed pond water with TWW effluents.

Sulphonamides (sulfamethoxazole, sulfamethazine and sulfapyridine, weakly acidic compounds with pKa 5-8) were always detected in monitored wells at lower concentrations in this study (Fig. 3, Table 2). They are widely used antibiotics in humans, and especially in veterinary medicine, as an antimicrobial substance in intensive livestock production to prevent and treat diseases. They have amphoteric properties, offer poor chelating ability and a low soil sorption tendency. Residues of sulphonamides have been detected in the groundwater located in the proximity of a confined animal-feeding operation (García-Galan et al., 2010). Sulfamethoxazole, also present in groundwater, is highly resistant to further biodegradation on the subsurface (Lam et al., 2004) and, consequently, it is minimally attenuated (Avisar et al., 2009; Fram and Belitz, 2011), mobile in saturated porous media presenting little influence to pH changes, ionic strength of solution and contradictory behaviour has been observed under different redox conditions (Chen et al., 2011; Banzhaf et al., 2012). It has a low K_{ow} (−0.1 to 1.7; Primor, 2008), is considerably hydrophilic and is also polar. Such properties enable sulfamethoxazole to be transported over long distances without being adsorbed to sediments (Lindsey et al., 2001; Perez et al., 2005). Furthermore under typical environmental pH conditions (pH ~7-8), it is negatively charged (95-100%; Primor, 2008) a property that can augment its transport velocity in porous media due to anion exclusion.

An attempt has been made to assess hydrochemical changes in the aquifer media taking into account Phs detection in RL1, RL2 and RL5 monitoring wells. In figure 4 groundwater and TWW concentration of some major and redox sensitive components (NO_3^-, O_2 and NH_4^+), carbamazepine, hydrochlorothiazide, 4-AAA, 4-FAA, sulphonamides and diclofenac have been plotted over time. Also as removal of many substances is redox-dependent, the time redox front and Cl^- concentration as indicator of the saline front movement breakthrough, have been plotted. Redox front was defined considering all sensitive components to redox changes in water (Chapelle, 2001).

Both hydrochemical processes, change from anoxic to oxic redox conditions and decrease of Cl^- concentration in the monitored wells due to dilution with the injected oxic TWW, took place at approximately 1 year after start of injection (2008). At the beginning of the injection period (2007), the NH_4^+ (reduced species) was present in saline water of wells at concentration close to 2 mgl^{-1} (RL1 and RL2) and greater than 15 mgl^{-1} (RL5); presence of oxidised species (e.g., NO_3^- and O_2) as a result of the TWW oxidation front was clearly observed after 2008 (Fig. 4). The increase of dissolved oxygen (up to 10 mgl^{-1}) was introduced by the injected TWW whereas nitrate was also produced by injected TWW but with an added surplus of ammonia oxidation. The groundwater oxic conditions appeared to be initially detected for wells RL2 and RL5 in June-July, and later (October) for RL1. The observed decrease of Phs concentration, appears to be more associate with the dilution process in the aquifer media than other transformation or degradation processes, fact also reported by other researchers (Laws et al., 2011).

For the Phs only found in groundwater (Table 1), they are very common, non-prescription/regulated compounds (e.g. paranxanthine a metabolite of caffeine, or contrast agents). Their presence maybe related to their high excretion as unchanged drug (codeine), high consumption rate (paranxanthine) or persistence (organic iodine) and apparently although further research is needed, they are not affected by changing redox. They are believed to have been released in the aquifer recharge area before the TWW injection, and residues are still present in the aquifer system (according to Teijón et al., 2010 tracing groundwater recharge revealed absence of Tritium). Different mechanisms and sources may explain presence of Phs in groundwater, ranging from disposal of treated effluents (and sludge) to the land or to surface streams hydraulically connected to aquifers, as may happen in the Llobregat valley; the possible leakage from sanitary sewer infrastructure in the boundary delta areas where only one aquifer exists, or, are thought to be the result of damaged wells connecting surface and deep aquifer. Illegal dumping in abandoned wells cannot be also discarded.

Conclusions

Artificial recharge, including injection through wells, can be generally considered a technique used in many parts of the world to enable the efficient use of non-conventional water resources that are currently not captured. However, it may also serve to transport pollutants into groundwater, especially highly polar molecules; occurrence may diminish with aquifer depth and distance from the injection wells. Although hydro-dispersive and reactive processes may diminish the original concentration of

Phs, aquifers may supply water containing these compounds and their metabolites for long periods (years-decades) as a consequence of low groundwater velocities, sluggish microbial activity and redox conditions.

At the study site, injected TWW significantly decreased Cl^- concentration in all monitored wells, showing a wider or narrower dilution range depending on the groundwater hydrochemical processes taking place and the hydraulic characteristics of the media. Redox process evolution in aquifer media by the mixing with injected TWW, led to changes from reduced species to oxidised species in groundwater following the oxidation front.

It was found that a full characterization and quantification of Phs in aquifer media is difficult and challenging due to the continuous injection of TWW, variability of compounds pattern consumption along time and entrance pathways into groundwater systems. Transformation products where not analysed within this study, however, their possible presence may be relevant when the parent compound presence is not observed in any evaluate sample. The newly detected pharmaceuticals are generally polar compounds with weak acid/basic characteristics, with behaviour influenced by its dissociation in water. Compounds fell within the concentration range of ngl^{-1} and the results indicate that some may remain detectable in the wells located at a distance of around 1 km from the injection locations. The different concentration values found in the monitoring wells appear to be driven by distance from recharge wells, dilution processes in the aquifer media and to the hydraulic parameters that govern flow, with attenuation or degradation being much less important due to prevailing subsurface hydrochemical conditions.

Although fate of Phs are determined by aquifer chemical and biological conditions and results from one system may not apply to other systems, obtained results may give important information for water resources management on fate of persistent compounds in subsurface media (Malamis et al. 2015).

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Figures and table captions

Table 1. Selected pharmaceuticals, CAS number and use analysed in the water sampled. Compounds detected in at least one water sample.

Table 2. Pharmaceuticals detected in groundwater (RL1, RL2, RL3 and RL5 wells) and injected water (TWW) at concentration greater than 0.1 μgl^{-1}, in at least one sample. The minimum, maximum and mean values considering all wells are also presented for the monitored period. (Due to the absence of regulated limits for this type of compounds, the concentration of 0.1 μgl^{-1}has been considered as a threshold value in this study).

Fig 1. Study site location and geologic cross-section of the delta aquifer. Injection wells (P1 to P4) and monitoring wells (RL1, RL2, RL3 and RL5) are also shown.

Fig. 2. Changes of HCO_3^- and $SO4^=$ versus Cl^- in the monitored wells (RL1, RL2 and RL5) and sampling campaigns during the study period (2007-2010).

Fig. 3. Stiff diagrams for selected monitoring wells: aquifer background (left diagram) and the last sampling campaign (right diagram).

Fig.4. Presence in the aquifer media and TWW of carbamazepine, diclofenac, hydrochlorothiazide and sulfonamides (sulfamethoxazole , sulfamethazine, sulfapyridine), 4-AAA, 4-FAA and O_2, NO_3^-, NH_4^+ and Cl^- for the study period. The oxidation front from TWW injection is also shown.

Figure 1
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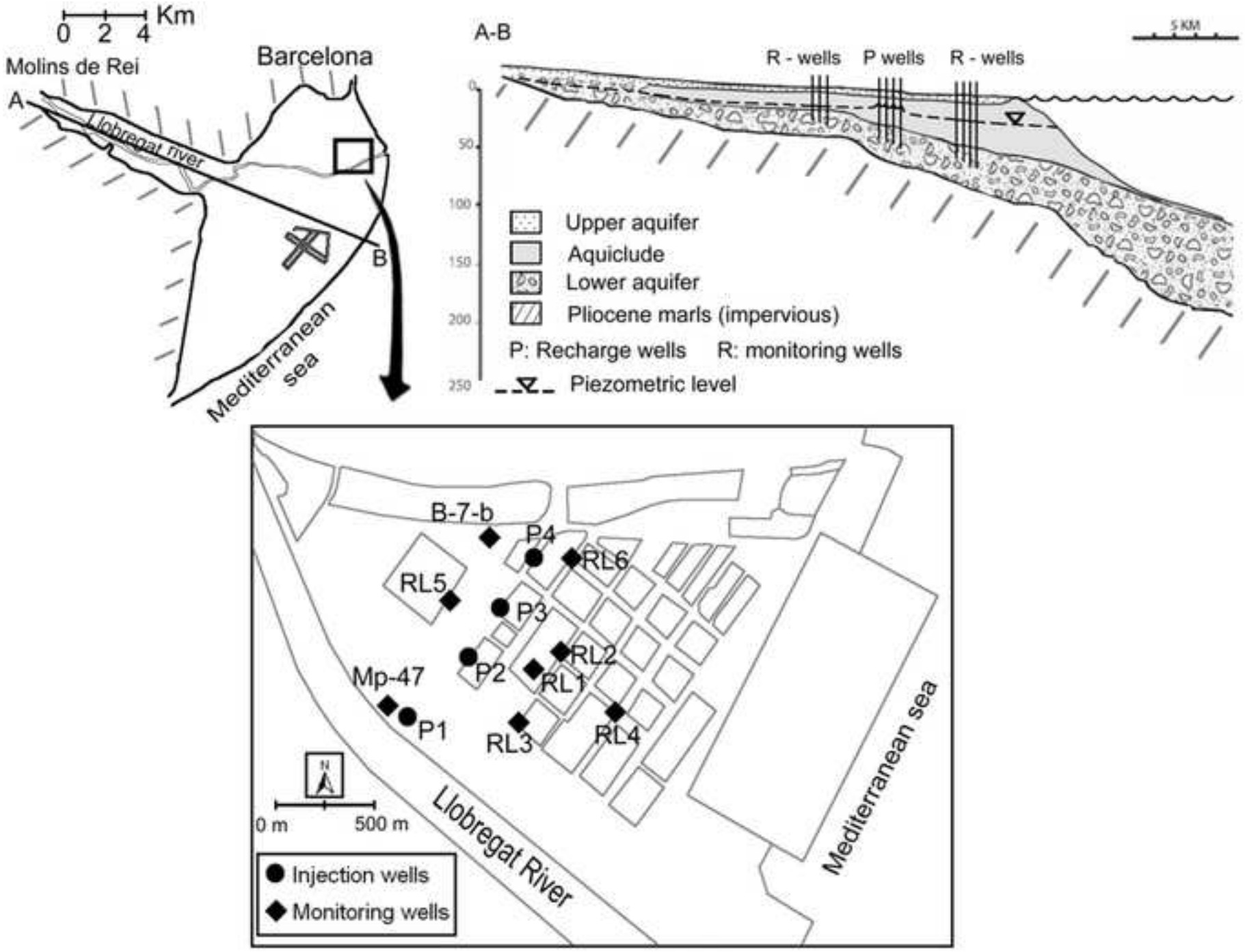

Figure 2
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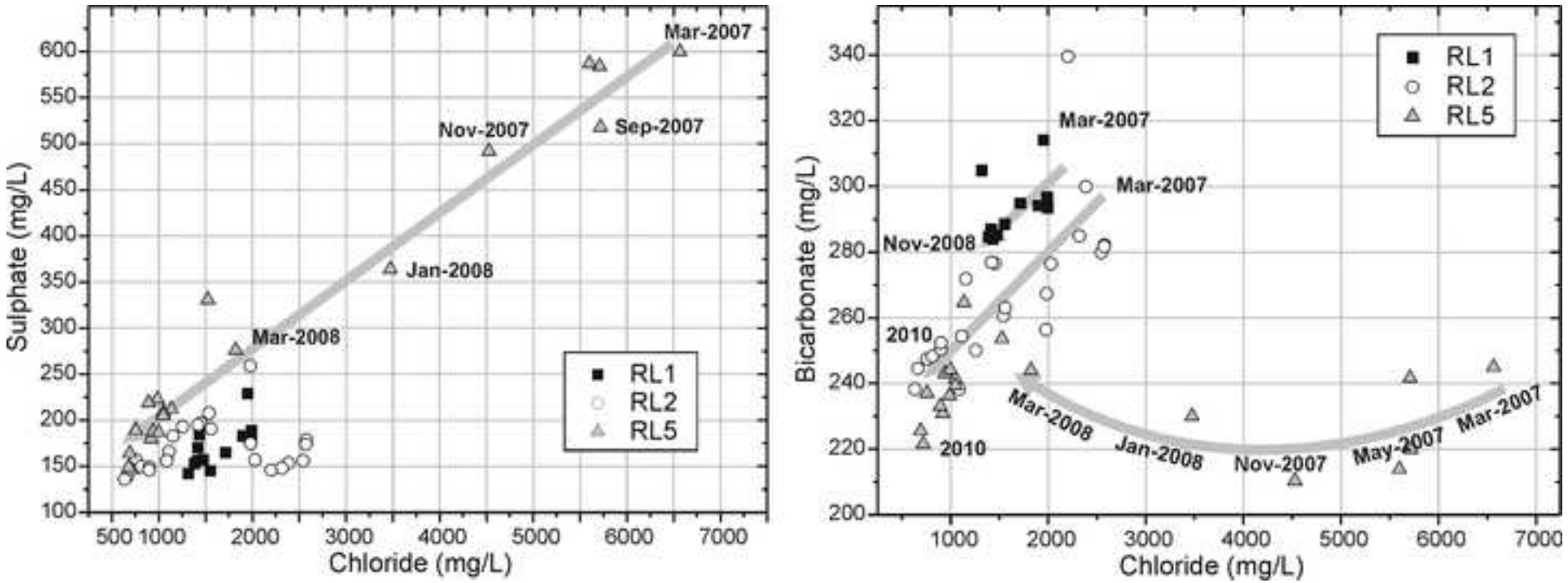

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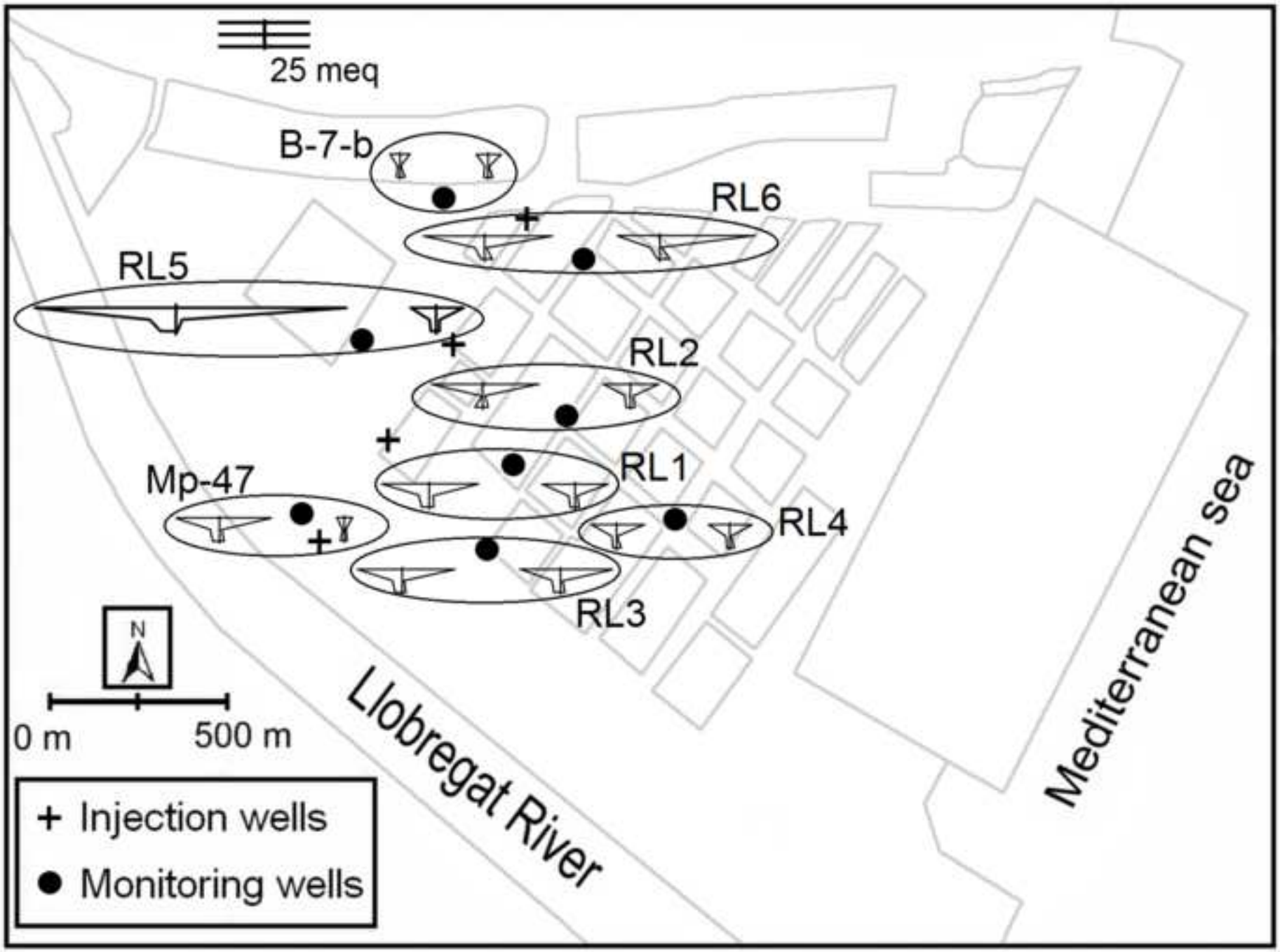

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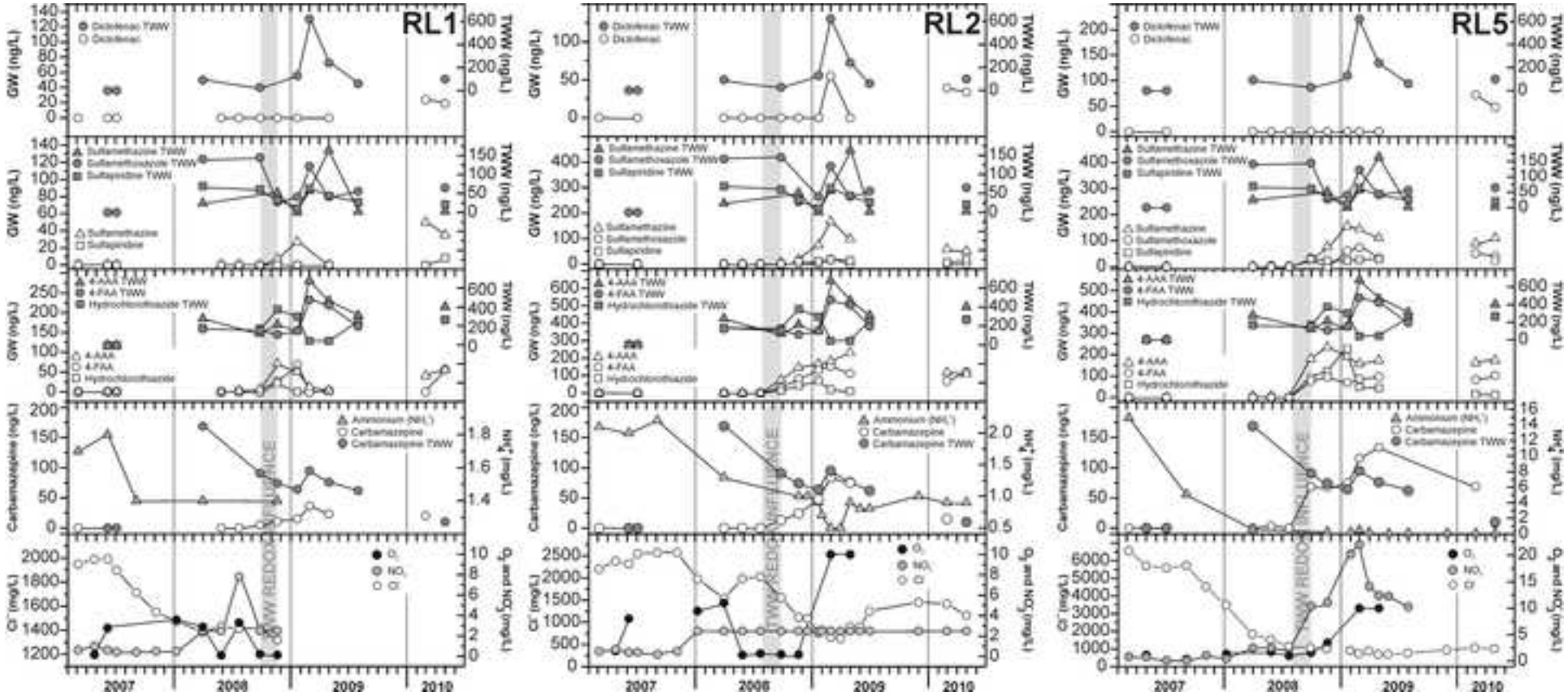

Table1

Compound	CAS number and use
4-amino-antipyrine (4-AA) **(*d*)**	83-07-8 Analgesic and anti-inflammatory
4-dimethylaminoantipyrine (4-DAA) (***ND)***	58-15-1 Analgesic, anti-inflammatory and antipyretic
4-MAA **(*d*)**	519-98-2 Metabolite of dipyrone
Acetaminophen ***(c)***	103-90-2 Analgesic
Amitriptyline ***(c)***	50-48-6 Antidepressant
Amoxicilin (***ND)***	26787-78-0 Antibiotic
Antipyrine **(*b*)**	60-80-0 Analgesic
Atenolol **(*b*)**	29122-68-7 Cardioselective beta-adrenergic blocker
Azithromycin ***(c)***	83905-01-5 Antibiotic
Bezafibrate **(*b*)**	41859-67-0 Peroxisome proliferator and hypolipidaemic agent
Caffeine **(*b*)**	58-08-2 Central nervous system stimulant
Carb,Epoxide **(*b*)**	36507-30-9 Metabolite of carbamazepine
Carbamazepine **(*b*)**	298-46-4 Anticonvulsant
Cefotaxime **(*b*)**	63527-52-6 Anti bacterial agent
Ciprofloxacin **(*b*)**	85721-33-1 Antibiotic
Citalopram **(*b*)**	59729-33-8 Antidepressant
Clarithromycin **(*b*)**	81103-11-9 Antibiotic
Clofibric acid **(*b*)**	882-09-7 Herbicide
Clomipramine (***ND)***	303-49-1 Antidepressant
Clotrimazole (***ND)***	23593-75-1 Antimycotic activity
Codeine **(*d*)**	76-57-3 Analgesic agent
Cotinine **(*b*)**	486-56-6 Metabolite of nicotine
Cyclophosphamide (***ND)***	50-18-0 Antineoplastic and immunosuppressive agent
Diatrizoate (***ND)***	117-96-4 X-ray contrast medium
Diazepam **(*b*)**	439-14-5 Anticonvulsant, anxiolytic, sedative, muscle relaxant, and amnesic properties
Diclofenac **(*b*)**	15307-86-5 Anti-inflammatory
Erythromycin **(*b*)**	114-07-8 Antibiotic
Famotidine (***ND)***	76824-35-6 Histamine H2-receptor antagonist
Fenofibrate **(*b*)**	49562-28-9 Antilipemic
Fenofibric acid **(*b*)**	42017-89-0 Metabolite of fenofibrate
Fenoprofen **(*d*)**	31879-05-7 Anti-inflammatory analgesic and antipyretic
Fluoxetine (***ND)***	54910-89-3 Antidepressant
Furosemide **(*b*)**	54-31-9 Diuretic
Gemfibrozil **(*b*)**	25812-30-0 Lipid-regulating
Hydrochlorothiazide **(*b*)**	58-93-5 Diuretic
Ibuprofen **(*d*)**	15687-27-1 Anti-inflammatory agent
Ifosfamide **(*b*)**	3778-73-2 alkylating agent and an immunosuppressive agent
Indomethacin **(*b*)**	53-86-1 Anti-inflammatory
Iopamidol **(*d*)**	62883-00-5 Contrast agent
Iopromide **(*d*)**	73334-07-3 Contrast agent

(b): detected in TWW and groundwater; ***(c)***: detected only in TWW; ***(d)****:* detected only in groundwater; **(*ND)***: not detected

Compound	CAS number and use
Ketoprofen **(*b*)**	22071-15-4 Anti-inflammatory analgesic and antipyretic
Ketorolac **(*d*)**	74103-06-3 Anti-Inflammatory
Lansoprazole (***ND)***	103577-45-3 Anti-Infective, antiulcer agent
Lincomycin **(*b*)**	154-21-2 Antibiotic
Loratadine **(*d*)**	79794-75-5 Antihistamines
Mefenamic acid **(*b*)**	61-68-7 Analgesic, anti-inflammatory, and antipyretic
Mepivacaine **(*b*)**	96-88-8 Local anesthetic
Methylprednisolone 6-alpha sodium succinate (***ND)***	2375-03-3 Anti-inflammatory
Metoprolol **(*b*)**	37350-58-6 Adrenergic beta-1-blocking agent
Metronidazole **(*b*)**	443-48-1 Antibiotic
Mevastatin (***ND)***	73573-88-3 Antibiotic, antifungal
N-acetyl-4-amino-antipyrine (4AAA) **(*b*)**	83-15-8 Metabolite of metamizol
Nadolol (***ND)***	42200-33-9 Cardiovascular disease
Naproxen **(*b*)**	22204-53-1 Anti-inflammatory agent with analgesic and antipyretic properties
N-formyl-4-amino-antipyrine (4FAA) **(*b*)**	1672-58-8 Metabolite of metamizol
Nicotine **(*b*)**	54-555-5 Insecticide, tobacco ingredient
Norfloxacin **(*b*)**	70458-96-7 Antibacterial
Ofloxacin **(*b*)**	82419-36-1 Antibacterial
Omeprazole **(*b*)**	73590-58-6 Inhibitor of gastric acid secretion
Paraxanthine ***(d)***	611-59-6 Central nervous system stimulant. Metabolite of caffeine
Paroxetine (***ND)***	61869-08-7 Serotonin uptake inhibitor, depression treatment
Phenacetin (***ND)***	62-44-2 Analgesic
Pravastatin **(*d*)**	81093-37-0 Antilipemic fungal metabolite
Primidone **(*b*)**	125-33-7 Antiepileptic
Propanolol hydrochloride **(*b*)**	525-66-6 Sympatholytic
Propyphenazone **(*b*)**	479-92-5 Anti-Inflammatory
Ranitidine ***(c)***	66357-35-5 Histamine H2-receptor antagonist
Salbutamol **(*b*)**	18559-94-9 Beta2-adrenergic agonist used to treat asthma
Salicilic acid **(*b*)**	69-72-7 Analgesic, antipyretic
Simvastatin (***ND)***	79902-63-9 Rate-limiting enzyme in cholesterol biosynthesis
Sotalol **(*b*)**	3930-20-9 Adrenergic beta-antagonist
Sulfadiazine **(*b*)**	68-35-9 Antibiotic
Sulfamethazine **(*b*)**	57-68-1 Antibacterial
Sulfamethoxazole **(*b*)**	723-46-6 Antibacterial
Sulfapyridine **(*b*)**	144-83-2 Antibacterial used to treat skin diseases
Sulfathiazole **(*b*)**	72-14-0 Anti-Infective agent
Tamoxifen (***ND)***	10540-29-1 Selective estrogen receptor modulator
Terbutaline (***ND)***	23031-25-6 Bronchodilator and tocolytic
Tetracycline (***ND)***	60-54-8 Antibiotic
Trimethoprim **(*b*)**	738-70-5 Bacteriostatic antibiotic
Venlafaxine **(*b*)**	93413-69-5 Antidepressant

Table 2

	TWW (ngl^{-1})			Groundwater (ngl^{-1})		
	Min	Max	Mean Value	Min	Max	Mean Value
Atenolol	24	218	104	5	106	47
Caffeine	10	141	40	4	505	73
Carbamazepine	10	169	82	3	134	46
Ciprofloxacin	-	52	-	2	406	126
Codeine	-	-	-	106	348	227
Diazepam	7	114	39	1	20	7
Diclofenac	29	622	182	19	74	49
Erythromycin	14	80	31	7	428	63
Furosemide	28	115	77	8	218	87
Gemfibrozil	7	716	203	12	852	255
Hydrochlorothiazide	2	301	165	2	228	50
Ibuprofen	-	-	-	-	185	185
Iopamidol	-	-	-	6	396	157
Iopromide	-	-	-	462	687	575
Mepivacaine	1	254	78	1	29	7
N-acetyl-4-amino-antipiryne (4-AAA)	76	678	299	3	236	111
Naproxen	37	476	233	103	263	170
N-formyl-4-amino-antipiryne (4-FAA)	110	478	229	27	162	96
Nicotine	11	155	37	5	190	50
Ofloxacin	3	516	220	3	178	43
Paraxanthine	-	-	-	23	147	79
Sulfamethazine	2	164	50	62	77	70
Sulfamethoxazole	28	145	82	4	18	9
Sulfapyridine	11	69	43	17	29	23
Velafaxime	82	196	138	2	181	104